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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,093	05/10/2001	Preeti G. Lal	PF-0357-1 DIV	8489

27904 7590 10/22/2003

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EXAMINER	
SHEINBERG, MONIKA B	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 10/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/854,093	LAL ET AL.	
	Examiner	Art Unit	
	Monika B Sheinberg	1634	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-20 and 35-37* is/are pending in the application.

4a) Of the above claim(s) *5-10,12-20 and 35-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-10,12-20 and 35-37* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1 sheet* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

DETAILED ACTION

Response Filed: July 15, 2003

Applicants' response to the Non-Responsive communication mailed June 20, 2003 indicates that the Non-Responsive communication was improper.

Election/Restrictions

Applicants' election with traverse of Group I (claims 1-4), directed to polypeptides, in the response filed April 14, 2003 is acknowledged. The traversal is on the ground(s) the restriction requirement was an "excessive restriction of claims, particularly with regard to compositions of matter and their methods of use" (p. 5 of the response). Applicants argue that the claims directed to the methods are within the same scope with respect to the composition of matter thus would not be an undue search burden upon the examiner. Thus Applicants requested the composition of matter and the methods of its use be rejoined. The applicants request the rejoinder of Groups I, III, VII and VIII (claims 1-4, 8, 15 and 16) in addition to the new claims 35-37. Applicants' request is acknowledged due to the election of claims directed to a product, and upon allowance of the product claims, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.3.12.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 USC 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined.

See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 USC § 103(b)," 1184 OG 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 USC 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See § 804.21. [Please note however, that claim 8 of the instant application, if rejoined, will be in conflict with claim 9 of the US Patent 6,232,459 (application 08/904,234).]

The cancellation of claims 11-14 and 21-34 is acknowledged. Claims 5-10, 15-20 and 35-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicants timely traversed the restriction (election) requirement in the response filed April 14, 2003. It is noted that newly added claims 36 and 37 are drawn to non-elected inventions, therefore also withdrawn from further consideration.

- Claims 1-10, 15-20 and 35-37 are pending.
- Claims 1-4 are hereby examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

- Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Lack of Written Description: The claims are broadly drawn to polypeptides comprising (a) an amino acid sequence of SEQ ID NO: 1; (b) naturally occurring amino acid sequences having 95% identity to any amino acid sequence within SEQ ID NO: 1 or the entirety of the amino acid sequence according to SEQ ID NO: 1; (c) a biologically acitive fragment or immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO: 1. Such recitation encompasses an extremely large genus of mutants, variants, and homologs of SEQ ID NO: 1, from any source in view of the broadest reasonable interpretationof the teachings in the specification.

The specification teaches the amino acid sequence SEQ ID NO: 1, which has 71% identity to the 28kDa isoform of the rat synaptojanin. The specification describes that the 28kDa peptide is a fragment of the 170kDa isoform that alters properties of the synaptojanin when combined with the 145kDa isoform. However, the specification does not teach how the 28kDa alone behaves. Thus, the specification teaches a fragment of a whole protein that has (as a fragment) 71% identity to a fragment of the rat 28kDa isoform of synaptojanin. The specification bases its description of SEQ ID NO: 1 on homology and predictive analyses such as the region of amino acids that may carry characteristics that "may represent" a signal peptide, "potential" membrane attachments, various "potential" protein kinase phosphorylation sites, and "potential intramolecular disulfide bonding sites as related to the rat isoform of synptojanin (SEQ ID NO: 3) which "shares an identity of 71%" (page 12 lines 1-25). The specification does not disclose and fully characterize any variants of these proteins, which have the same biological activity or a different biological activity. No proteins are exemplified which have 95%, 96% etc. identity with SEQ ID NO: 1. The specific 5% that are not identical to the elected sequence are represented by the claim are not supported by the specification. The specification does not provide guidance as to which sequences to alter to retain a functional variant besides retaining a function that remains consistent with that of SEQ ID NO: 1 as a part of the 170kDa isoform of synaptojanin or separately from the 170kDa isoform. The specification has not taught or demonstrated those sequences of SEQ ID NO: 1 that are responsible for biologically activity thus a skilled artisan would be unable to determine what portion of the sequence is required by size and location to retain a biologically active fragment. The specification teaches that SEQ ID NO: 1 is expressed in inflamed tissues (rheumatism and Crohn's disease) and epilepsy on page 12

(lines 20-25), however has not defined the actual biological activity or function of SEQ ID NO: 1 and thereby encompass polypeptides having any biological activity. Thus the breadth of these claims encompass a large genus of mutants, variants and homologs of SEQ ID NO: 1, from any source, that have not been taught or described by the specification. The recitation of a single sequence is not representative of this large genus of peptides. While one of skill in the art could argue that the claimed genus of polypeptide is adequately described since one can isolate these polynucleotide (from which SEQ ID NO: 1 is encoded) by sequence comparison using the polypeptide/polynucleotide structures disclosed in the instant application or the prior art, the state of the art teaches that sequence comparison alone should not be used to determine a protein's function and that small amino acid changes can drastically change the function of a polypeptide. Bork [Genome Research, 10: 398-400 (2000)] teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Van de Loo et al. [PNAS 92; 6743-6747 (1995)] teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* were found to be hydroxylases once tested for activity. Seffernick et al. [J. Baceriol. 183 (8); 2405-2410 (2001)] teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. [Science 282: 1315-1317 (1998)] teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydroxylase and as few as six amino acid substitutions can transform a hydroxylase to a desaturases. The genus of polypeptides comprised by the claim is a large variable genus, which can potentially be proteins of diverse functions. The specification only discloses a single species of the genus, i.e. the polypeptide of SEQ ID NO: 1, which is insufficient to put one of skill in the art in possession of all attributes and features of all species within the genus. Thus one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons

of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 1; the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotide, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Therefore, only SEQ ID NO: 1, but not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision.

As stated above, the following of claim 1 recite limitations to SEQ ID NO: 1 which are not present within the disclosed SEQ ID NO: 1. Step (b) requires that (emphasis added) "at least

95% sequence identity to **an** amino acid sequence **of** SEQ ID NO: 1" thereby a 95% identity to any portion of SEQ ID NO: 1. No function and/or region has been identified within SEQ ID NO: 1 that is required to maintain 95% identity in order to retain functionality. Step (c) requires a biologically active fragment (or immunogenic fragment) of an amino acid sequence of SEQ ID NO: 1. Again, no function and/or region of the sequence has been identified within SEQ ID NO: 1 to be biologically active or carry a specific biological function.

- Claim 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPA 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

The claims are not enabled for "biologically active fragments" of the polypeptide SEQ ID NO: 1 (NYSN-1) with the characteristics of the instant claims. The specification teaches the amino acid sequence SEQ ID NO: 1, which has 71% identity to the 28kDa isoform of the rat synaptojanin. The specification describes that the 28kDa peptide is a fragment of the 170kDa isoform that alters properties of the synaptojanin when combined with the 145kDa isoform. However, the specification does not teach how the 28kDa alone functions. Thus, the specification teaches a fragment of a whole protein that has (as a fragment) 71% identity to a fragment of the rat 28kDa isoform of synaptojanin. The specification bases its description of SEQ ID NO: 1 on homology and predictive analyses such as the region of amino acids that may carry characteristics that "may represent" a signal peptide, "potential" membrane attachments,

various "potential" protein kinase phosphorylation sites, and "potential intramolecular disulfide bonding sites as related to the rat isoform of synptojanin (SEQ ID NO: 3) which "shares an identity of 71%" (page 12 lines 1-25). These potential regions or residues do not give them all the same function or ascribe a predictable function to the protein with only such minimal information. The specification thus has taught potential physical characteristics, however the specification has not taught where and how to modify the polypeptide to produce a protein with the same or potentially the same functionality. The specification does not provide guidance as to which sequences to alter to retain a functional variant besides retaining a function that remains consistent with that of SEQ ID NO: 1 as a part of the 170kDa isoform of synaptojanin or separately from the 170kDa isoform. The specification has not taught or demonstrated those sequences of SEQ ID NO: 1 that are responsible for biologically activity thus a skilled artisan would be unable to determine what portion of the sequence is required by size and location to retain a biologically active fragment. The specification teaches that SEQ ID NO: 1 is expressed in inflamed tissues (rheumatism and Crohn's disease) and epilepsy on page 12 (lines 20-25), however has not defined the actual biological activity or function of SEQ ID NO: 1 and thereby the claims encompass polypeptides having any biological activity. The instant claims are drawn to undisclosed sequences encoding any modification that have not been contemplated. While the specification teaches the amino acid sequence of the human synaptojanin isoform (NSYN-1; similar to the 28kDa rat isoform) isolated in this invention, one sequence does not enable a genus of synaptojanin molecules based on the potential physical characteristics disclosed in the instant application. Therefore, the artisan would be required to perform undue experimentation to identify any polypeptide which was an active fragment of the synaptojanin as a portion (28kDa) of the presently claimed invention or as a whole (when in combination with 145kDa). The skilled artisan would have no way of knowing which polypeptide sequences were "active fragments" of NSYN-1 because the specification does not provide a description of the amino acid sequences which constitute these "active fragments". The skilled artisan would be required to perform manipulations and extensive modification of the protein to determine where and how to make modifications to determine which fragments of the polypeptide were responsible for it's activity.

As indicated above, the claim encompasses polypeptides, which can potentially are proteins of diverse function. With respect to claims 3 and 4, applicant contemplates the use of these sequences in addition to the whole SEQ ID NO: 1, in a composition directed (as indicated by the specification) to cancer and immune disorders which in effect encompass a method of treatment for which the instant application is not enabled. The specification does not teach how to use or what portions of SEQ ID NO: 1 to use in order to be "effective" in treatment. The specification does not teach what amount of SEQ ID NO: 1 would be effective in the composition or for what the effectiveness is directed to. The specification teaches that SEQ ID NO: 1 is expressed in inflamed tissues (rheumatism and Crohn's disease) and epilepsy on page 12 (lines 20-25), however has not defined the actual biological activity or function of SEQ ID NO: 1 and thereby the claims encompass polypeptides having any biological activity such that the skilled artisan would not be enabled to produce a composition that would contain an effective amount of any polypeptide encompassed by the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

- Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "effective" in claim 3 is a relative term which renders the claim indefinite. The term "effective" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claim 4 is also indefinite due to dependency from claim 3.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by the 1993 Sigma Chemical Catalogue product P 2254.

In the 1993 Sigma Chemical Catalog product P 2254 is a poly-proline which has 100% identity to the fragment of poly proline amino acid residues 270-274 of SEQ ID NO: 1. The sequence thus anticipates the instant claims 1-3 via fragments, which consist of an amino acid sequence of SEQ ID NO: 1.

- Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Mochizuki et al (US Patent 5,395,916; March-1995).

Mockizuki et al (column 8, lines 13-65) teaches a pharmaceutical composition containing an amino acid sequence of poly-proline. The poly-proline is identical to the fragment of poly-proline amino acid residues 270-274 of SEQ ID NO: 1 and is comprised in an effective amount for a pharmaceutical composition (claim 3).

Conclusion

- Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph – lack of written description.
- Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph – scope of enablement.
- Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph.
- Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by the 1993 Sigma Chemical Catalogue product P 2254.
- Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Mochizuki et al.

No claim is allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The central **Fax number is (703) 872-9306**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 9 A.M to 5 P.M. If attempts to reach the examiner by

telephone are unsuccessful, the primary examiner in charge of the prosecution of this case, Jehanne Souaya, can be reached at 703-308-6565. If attempts to reach the examiners are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Chantae Dessau, whose telephone number is (703) 605-1237, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

October 20, 2003
Monika B. Sheinberg
Art Unit 1634

MBS

JEHANNE SOUAYA
PATENT EXAMINER
Jehanne Souaya
10/20/03